SCIENTIFIC ABSTRACT

Human effector cells are capable of killing tumor cells in vitro under appropriate conditions. Several of those killer cells have been identified as NK cells, LAK cells, macrophages, and T cells. These effector cells have in common that they respond to Interleukin-2 (IL-2). The most powerful effector cell populations are the T cells. It is the only cell population characterized by memory and specificity and the capability to migrate from one tumor deposit to the next one destroying tumor cells until the last cancer cells are gone. $CD8^+$ cells play the predominant role for lysing tumor cells. $CD8^+$ T cells are usually MHC class I restricted and recognize octamers or nanomers assembled in the groove of the MHC class I molecule. Interferon-γ (IFNγ) upregulates MHC and adhesion molecules on the cell surface and makes tumor cells more visible to T cells. Intracellular tumor associated antigens (TAA) must be processed before being presented by MHC class I molecules to $CD8^+$ T cells. Frequently tumor cells have defects in antigen presentation. In several instances these defects were reversible by IFNγ. The observation that IL-2 stimulates CD8 cells and IFNγ upregulates MHC molecules and reverses defects in antigen presentation makes a combination of these molecules very attractive for gene therapy approaches to cancer.

We are planning to study LNCAP/IL2/IFNγ, a prostate carcinoma cell line transduced with a retroviral vector carrying both the human IFN-γ and IL-2 cDNA. This cell line will be characterized and then used as a vaccine in patients with prostate carcinoma as an allogeneic HLA class I matched vaccine.